

Exhibit 9

In The Matter Of:

ARIOSIA DIAGNOSTICS, INC.

v.

SEQUENOM, INC.

EVANS, M.D., MARK I. - Vol. 1

April 27, 2012

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MERRILL CORPORATION

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UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

--oOo--

ARIOSIA DIAGNOSTICS, INC.,
(aka ARIA DIAGNOSTICS),

Plaintiff,

Case No.
3:11-cv-06391-SI

v.

SEQUENOM, INC.,

Defendant/
Counterclaim-Plaintiff.

v.

ARIOSIA DIAGNOSTICS, INC.,
(aka ARIA DIAGNOSTICS),

Counterclaim-Defendant,

and

ISIS INNOVATION LIMITED,

Nominal Counterclaim-
Defendant.

_____/

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VIDEOTAPED DEPOSITION OF
MARK I. EVANS, M.D.

Friday, April 27, 2012

Volume I (Pages 1 - 258)

REPORTED BY: CATHERINE RYAN, RMR, CRR, CSR 8239

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1 process and use free fetal nucleic acids was 12:18:54
2 possible. This was believed to be absolutely 12:19:00
3 impossible up until that paper emerged. 12:19:03

4 Q And if you look, however, to the patent, 12:19:12
5 the '540 patent -- and you mentioned getting the 12:19:15
6 plasma and getting to amplify and to detect the 12:19:21
7 presence of paternally inherited nucleic acids of 12:19:26
8 fetal origin. If you look at the patent and the 12:19:30
9 claims, they don't specify how you do all those 12:19:36
10 things; isn't that right? 12:19:39

11 MR. HOLMES: Objection. Vague. Compound. 12:19:41

12 THE WITNESS: The patent gives a number of 12:19:43
13 examples of how you do these things. 12:19:49

14 BY MR. IANCU: 12:19:50

15 Q But -- but -- 12:19:51

16 A The -- I'm not a patent lawyer. The 12:19:52
17 patent propo -- makes claims which proposes 12:19:54
18 methodologies for how these claims can be effected. 12:20:01
19 There are some five examples as to how this 12:20:07
20 technology can be used, which are not limiting, but 12:20:09
21 certainly instructive as to how it can be used, and 12:20:14
22 the fact that any of this could be done was, to 12:20:19
23 those of us, quite frankly, at the forefront of the 12:20:24
24 attempt to develop noninvasive prenatal diagnosis 12:20:28
25 methods came as a complete shock. 12:20:32

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1 And what I was starting to say before we 12:20:35
2 got sidetracked a minute ago was that I remember 12:20:37
3 sitting at one of our three-times-a-year, 12:20:40
4 twice-a-year big group meetings shortly after the 12:20:45
5 paper came out and, you know, Dr. Bianchi, 12:20:48
6 Dr. Elias, Dr. Holzgreve and myself basically all 12:20:54
7 being what I would describe as shellshocked that 12:20:59
8 there was another and quite possibly much better way 12:21:01
9 of doing this than we had all spent a decade or more 12:21:03
10 working on, you know, within fetal cells, which 12:21:08
11 produced a lot of frustration. 12:21:11

12 Q And that's the discovery that fetal cells 12:21:13
13 exist in the plasma, right? 12:21:22

14 A No, we knew fetal cells existed in the 12:21:24
15 plasma in small numbers. The problem with fetal 12:21:28
16 cells was being able to use them accurately for 12:21:31
17 diagnosis. 12:21:33

18 Q How would a person of skill in the art 12:22:06
19 know in 1997 how you would, for example, amplify 12:22:12
20 paternally inherited nucleic acids from the serum or 12:22:20
21 plasma? 12:22:24

22 MR. HOLMES: Let me just interpose an 12:22:26
23 objection to the extent it calls for a legal 12:22:27
24 conclusion and vague. 12:22:29

25 BY MR. IANCU: 12:22:39

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1	Q	Do you have the question in mind, sir?	12:22:40
2	A	Yes. The technique of the polymerase	12:22:41
3		chain reaction was already well known in science at	12:22:46
4		that time as well as other methodologies which could	12:22:49
5		be used. So it was known that if one had paternally	12:22:55
6		derived nucleic acids of fetal origin, that one	12:23:04
7		could amplify them, at least in principle.	12:23:07
8	Q	And how would a person of skill in the art	12:23:29
9		know in 1997 how to detect the presence of a	12:23:32
10		paternally inherited nucleic acid of fetal origin in	12:23:38
11		the sample?	12:23:42
12		MR. HOLMES: Same objections.	12:23:43
13		THE WITNESS: I'm sorry. Could you repeat	12:23:47
14		the question, please?	12:23:48
15		BY MR. IANCU:	12:23:49
16	Q	How would a person of skill in the art in	12:23:49
17		1997 know how to actually detect the presence of	12:23:52
18		paternally inherited nucleic acid of fetal origin in	12:23:57
19		serum or plasma --	12:24:03
20		MR. HOLMES: Same objections.	12:24:05
21		BY MR. IANCU:	12:24:05
22	Q	-- of the mother?	12:24:06
23	A	Dr. Lo's paper published in the Lancet --	12:24:07
24		and I'd like to get it before I -- do we have a copy	12:24:11
25		of it here someplace? Okay. Dr. Lo's paper	12:24:13

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1	described methodology for -- for isolating maternal	12:24:19
2	plasma and then amplifying those sequences and then	12:24:37
3	detecting the presence of those acids.	12:24:42
4	Q Now, isolating maternal plasma is known	12:24:47
5	for a very long time, well before 1997, right?	12:24:51
6	A That one component is certainly known,	12:24:54
7	yes.	12:24:57
8	Q How do you do it, by the way?	12:24:57
9	A Basically, you can take a tube of blood	12:25:00
10	and just stick it on the table and it will clot off.	12:25:04
11	And then if you spin it, you get serum. If you	12:25:06
12	give anticoagulant so that the clotting factors	12:25:09
13	don't clump the cells, you get plasma. And then you	12:25:12
14	centrifuge it; so you separate out the cellular from	12:25:16
15	noncellular portions.	12:25:19
16	Q So taking the plasma, the maternal plasma,	12:25:25
17	if you know that you want to look in there for	12:25:28
18	paternally inherited nucleic acids of fetal origin,	12:25:30
19	how would one know what techniques to use? Was	12:25:34
20	there anything available how to do that, the actual	12:25:38
21	technology --	12:25:41
22	MR. HOLMES: Objection. Vague.	12:25:42
23	BY MR. IANCU:	12:25:43
24	Q -- in 1997?	12:25:44
25	A There are techniques that were being	12:25:52

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1 developed in molecular biology, which obviously 12:25:53
2 Dr. Lo used, but nobody thought to apply them. The 12:26:05
3 -- what we always did in the fetal cells in maternal 12:26:07
4 blood effort was to basically keep the cells and 12:26:08
5 throw away everything else, and, in fact, we were 12:26:09
6 throwing the baby away with the bath water. 12:26:13

7 Q But once you know that you want to look 12:26:18
8 for paternally inherited nucleic acids of fetal 12:26:20
9 origin in the maternal serum or plasma in 1997, 12:26:25
10 wouldn't one of ordinary skill in the art actually 12:26:30
11 have to engage in lots of experimentation to 12:26:33
12 actually, from that point forward, to figure out how 12:26:35
13 to do it? 12:26:38

14 MR. HOLMES: Objection. Vague. Lacks 12:26:38
15 foundation. 12:26:39

16 THE WITNESS: Well, I'm sure that Dr. Lo 12:26:41
17 didn't wake up one morning and have the solution 12:26:45
18 figured out by lunchtime, that the sentinel 12:26:49
19 discovery was the fact that these materials were 12:26:55
20 there in the first place combined with the fact that 12:26:58
21 one could then find them, isolate them and use them. 12:27:02
22 So it's all the big picture. 12:27:06

23 BY MR. IANCU: 12:27:07

24 Q But how would you find them? How would 12:27:08
25 you find them in 1997? 12:27:10

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1	A	By having probes against, for example, the	12:27:11
2		Y chromosome --	12:27:17
3	Q	And --	12:27:19
4	A	-- sequences, which, of course, would not	12:27:20
5		be expected to be in a maternal sample or a -- with	12:27:22
6		a female fetus.	12:27:26
7	Q	Would anyone know how -- how to use probes	12:27:27
8		against the Y chromosome, as an example, in 1997?	12:27:33
9		MR. HOLMES: Objection. Vague.	12:27:39
10		THE WITNESS: Sure. That's exactly what	12:27:40
11		we were attempting to do in the NIFTY project, that	12:27:40
12		we were isolating cells and trying to use Y	12:27:42
13		chromosome probes to show that those cells in the	12:27:47
14		maternal circulation were, in fact, fetal and,	12:27:50
15		therefore, of paternal origin.	12:27:52
16		BY MR. IANCU:	12:27:54
17	Q	And people were doing that for a while	12:27:55
18		prior to 1997?	12:27:57
19	A	People --	12:27:59
20		MR. HOLMES: Same objection.	12:28:00
21		THE WITNESS: People were looking for --	12:28:01
22		and I was part of the big NIH study. I was one of	12:28:02
23		the principal investigators, where we were looking	12:28:07
24		for fetal cells circulating in the maternal	12:28:10
25		circulation and trying to find probes that could be	12:28:15

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1 used to distinguish those cells in the maternal 12:28:20
2 circulation that came from the fetus as opposed to 12:28:25
3 that came from the mother. 12:28:28

4 BY MR. IANCU: 12:28:31

5 Q Once you know where you want to look for 12:28:31
6 the fetal cells, now that you want to look in the 12:28:35
7 plasma, for example, per Dr. Lo's 1997 paper, once 12:28:39
8 you know that -- 12:28:44

9 A No, that's incorrect. 12:28:44

10 Q Apologies. Go ahead. 12:28:45

11 A Sorry. 12:28:47

12 MR. HOLMES: Dr. Evans, let -- 12:28:47

13 THE WITNESS: I apologize. 12:28:49

14 MR. HOLMES: -- Mr. Iancu finish his 12:28:49
15 question. 12:28:53

16 THE WITNESS: Fair enough. 12:28:55

17 BY MR. IANCU: 12:28:55

18 Q I can often be incorrect; so I appreciate 12:28:56
19 you correcting me. 12:28:57

20 A Well, you said "fetal cells," not fetal 12:28:59
21 DNA. 12:29:01

22 Q Yes. Good. Thank you. I'm sorry. 12:29:01

23 Once you know where you want to look for 12:29:03
24 fetal DNA in the material -- in the maternal plasma, 12:29:05
25 as an example from -- per Dr. Lo's 1997 paper, the 12:29:10

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1	techniques for how to look for that DNA, how would	12:29:22
2	one of skill in the art know of those techniques at	12:29:35
3	that time?	12:29:36
4	MR. HOLMES: Objection. Vague.	12:29:37
5	THE WITNESS: Techniques such as the	12:29:39
6	polymerase chain reaction were known in the field at	12:29:40
7	that point.	12:29:43
8	BY MR. IANCU:	12:29:43
9	Q And with that you can use to detect DNA,	12:29:44
10	correct?	12:29:47
11	A Yes.	12:29:47
12	Q Now, in your report at paragraph 47	12:29:50
13	through 50 you describe a variety of awards and	12:30:33
14	honors that you believe Dr. Lo received; is that	12:30:41
15	right?	12:30:44
16	A That's correct.	12:30:45
17	Q Go ahead and take a quick look through	12:30:46
18	that. I'll have a couple of questions on that.	12:30:50
19	A Okay.	12:30:53
20	Q My question, Dr. Evans, is: Specifically,	12:31:12
21	do you know what all of these awards were for in	12:31:21
22	paragraph 47, for example?	12:31:23
23	A I do not know specifically what they were	12:31:43
24	for.	12:31:47
25	Q Okay. So in paragraph 50 you indicated	12:31:49

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1	Dr. Lo is a reviewer for these following journals.	12:31:59
2	How do you know all that?	12:32:02
3	A This information obviously came from	12:32:04
4	Dr. Lo.	12:32:07
5	Q Did you speak with Dr. Lo to prepare this	12:32:08
6	declaration?	12:32:11
7	A I'm finishing my question.	12:32:11
8	Q Your answer?	12:32:13
9	A My answer, okay. And was submitted to the	12:32:15
10	attorneys, okay? And this looked -- I had no reason	12:32:17
11	to doubt it and to be willing to state that this is	12:32:20
12	accurate, but I have no independent verification of	12:32:25
13	it.	12:32:28
14	Q Okay. You signed this declaration under	12:32:29
15	oath, penalty of perjury, right?	12:32:31
16	A Yes, and I know Dr. Lo to be a man of	12:32:32
17	integrity, and I refuse to believe that he would lie	12:32:35
18	about which awards he won. That's easily	12:32:37
19	verifiable.	12:32:40
20	Q All right. Do you know specifically what	12:32:42
21	articles or area of science Dr. Lo was reviewing in	12:32:49
22	these journals in paragraph 50?	12:32:54
23	A I don't know specifically. I know, since	12:32:57
24	I review for a number of these journals myself, they	12:32:59
25	tend to send you articles in your known area of	12:33:05

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1	I'm -- I can't play games with you like this. I	12:46:04
2	don't know.	12:46:07
3	BY MR. IANCU:	12:46:07
4	Q Take a look at paragraph 70 in your	12:46:45
5	report. My question is: On the second sentence	12:46:48
6	where you say, quote, "While researchers knew that	12:47:30
7	the very small number of fetal cells escape the	12:47:35
8	placenta, it was not known that cell-free DNA was	12:47:38
9	present in the maternal plasma in detectable	12:47:42
10	quantities," closed quote. Do you see that	12:47:45
11	sentence?	12:47:48
12	A Yes, I do.	12:47:48
13	Q Do you agree with that sentence?	12:47:49
14	A Yes.	12:47:50
15	Q Why wasn't it known that cell-free DNA was	12:47:57
16	present in the maternal plasma in detectable	12:48:01
17	quantities?	12:48:04
18	MR. HOLMES: Objection. Vague. Calls for	12:48:05
19	speculation.	12:48:06
20	THE WITNESS: Why haven't we cured cancer	12:48:07
21	yet? We --	12:48:10
22	BY MR. IANCU:	12:48:10
23	Q I don't know. That's not my question,	12:48:11
24	sir.	12:48:12
25	A Yes, it is because --	12:48:12

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1 Q Let me try, then -- let me ask a different 12:48:15
2 question. Who was it that made it known that 12:48:19
3 cell-free DNA was present in the maternal plasma in 12:48:20
4 detectable quantities? 12:48:24

5 A Dr. Lo and Wainscoat. 12:48:26

6 Q Anyone else? 12:48:32

7 A Dr. Lo and Wainscoat had the sentinel 12:48:34
8 discovery, which resulted in the Lancet paper, other 12:48:38
9 papers and ultimately in the patents in question and 12:48:43
10 are regarded in the field as the pioneers who found 12:48:46
11 this and learned how to use it when no one else in 12:48:51
12 the field actively working on it thought it could 12:48:57
13 possibly be done. 12:48:59

14 Q In the next sentence where you begin with 12:49:22
15 "Indeed," do you see that next sentence? 12:49:25

16 A Okay. 12:49:27

17 Q It ends with, quote, "Nobody thought that 12:49:28
18 fetal cell-free DNA would be present," closed quote; 12:49:31
19 do you see that? 12:49:39

20 A Yes. 12:49:44

21 Q Which you mean is that nobody thought that 12:49:45
22 fetal cell-free DNA would be present in the plasma? 12:49:46

23 A In the maternal plasma. 12:49:50

24 Q Right? Now, it was always there, right? 12:49:54

25 A We now understand that it was there. 12:50:01

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1	Q	Okay. Let's take a look at paragraph 72.	12:50:03
2		Go ahead and read that to yourself.	12:50:15
3	A	Okay.	12:50:58
4	Q	Can you please explain what you mean by	12:51:16
5		what's in paragraph 72?	12:51:17
6	A	Paragraph 72 is fundamentally a rehash of	12:51:21
7		the discussion that we had earlier this morning	12:51:25
8		where I talked about 100 units of A and 100 units of	12:51:29
9		B being the nonpregnant amount and that if a normal	12:51:33
10		fetus were contributing 10 percent, as is	12:51:39
11		articulated in paragraph 72, that one would then	12:51:43
12		expect 10 -- the 100 number to go to 110, but that	12:51:47
13		if there were a trisomy, one would expect it to go	12:51:56
14		to 115. So it's exactly the same principle as what	12:52:00
15		I've described here.	12:52:03
16	Q	You conclude that paragraph with a	12:52:13
17		sentence that says, quote, "This is a relatively	12:52:15
18		small increase in chromosome 21 to detect," closed	12:52:25
19		quote.	12:52:27
20	A	Yes.	12:52:27
21	Q	What do you -- what's the point you're	12:52:27
22		making there?	12:52:28
23	A	The point I'm making, which, again, is	12:52:28
24		something I had said earlier, is that, depending	12:52:29
25		upon the fetal fraction -- I used the analogy	12:52:33

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1	Q	Correct.	02:14:47
2	A	Yes, that's what I said.	02:14:47
3	Q	By the way, what is an oligonucleotide?	02:15:09
4	A	It is a nucleotide of a small number of	02:15:22
5		base pairs.	02:15:26
6	Q	In paragraph 101 you say that, "Nucleic	02:15:33
7		acid from the fetus is made up of nucleic acid that	02:15:49
8		was inherited from the father and nucleic acid that	02:15:52
9		was inherited from the mother," correct?	02:15:55
10	A	Yes.	02:16:00
11	Q	Is that all there is in nucleic acid from	02:16:08
12		the fetus?	02:16:12
13		MR. HOLMES: Objection. Vague.	02:16:15
14		THE WITNESS: I'm sorry. Please repeat	02:16:17
15		that.	02:16:18
16		BY MR. IANCU:	02:16:19
17	Q	Does fetal nucleic acid have to be	02:16:21
18		inherited either from the mother or the father?	02:16:25
19	A	If there is a de novo mutation, it could	02:16:32
20		be inherited from neither, but fundamentally	02:16:36
21		99.99 percent of a fetus's DNA will have come from	02:16:40
22		either the mother or the father.	02:16:45
23	Q	Nevertheless, there are situations where	02:16:47
24		fetal DNA is not inherited either from the mom or	02:16:48
25		the dad?	02:16:52

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1	A	Incredibly rare, but yes.	02:16:54
2	Q	Okay. Let's go to paragraph 104. Go	02:17:31
3		ahead and read that to yourself.	02:17:33
4	A	Okay.	02:17:58
5	Q	Others before Dr. Lo amplified and	02:18:39
6		detected nucleic acids, right?	02:18:42
7	A	Yes.	02:18:47
8	Q	In fact, traditional DNA diagnostics well	02:18:47
9		before 1997 traditionally involved three steps,	02:18:52
10		right: Sample preparation, amplification, and	02:18:58
11		detection, correct?	02:19:00
12		MR. HOLMES: Objection. Vague.	02:19:01
13		THE WITNESS: Commonly.	02:19:02
14		BY MR. IANCU:	02:19:03
15	Q	And the others before Dr. Lo amplified and	02:19:10
16		detected nucleic acid in plasma or serum, true?	02:19:12
17	A	Yes.	02:19:17
18	Q	And, actually, amplifying and detecting	02:19:24
19		nucleic acids was done using fetal cells in maternal	02:19:26
20		blood for years before the '540 patent, right?	02:19:32
21	A	Repeat that again, please.	02:19:34
22	Q	Amplifying and detecting nucleic acids was	02:19:37
23		done using fetal cells in maternal blood for years	02:19:41
24		before the '540 patent, correct?	02:19:43
25		MR. HOLMES: I'm going to object to the	02:19:45

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1 extent it calls for a legal conclusion. 02:19:47

2 THE WITNESS: Actually, we were not able 02:19:49

3 to amplify fetal cells in maternal blood. That was 02:19:50

4 part of the problem. Couldn't get them to grow. 02:19:54

5 BY MR. IANCU: 02:20:06

6 Q Right. So let me ask it again. I'm not 02:20:06

7 asking about fetal cells. I'm asking a different 02:20:10

8 question. 02:20:12

9 Amplifying and detecting nucleic acid was 02:20:13

10 done using fetal cells in maternal blood for years 02:20:18

11 before the '540 patent, right? 02:20:20

12 MR. HOLMES: Objection. Vague. 02:20:22

13 THE WITNESS: And I will give you the same 02:20:23

14 answer I just -- 02:20:25

15 MR. HOLMES: Also to the extent it calls 02:20:26

16 for a legal conclusion. 02:20:27

17 THE WITNESS: I will give you the same 02:20:28

18 answer I gave you before, that the attempt to 02:20:30

19 amplify fetal nucleic acids in the fetal cells was 02:20:35

20 unsuccessful. 02:20:40

21 BY MR. IANCU: 02:20:42

22 Q Fetal cells that existed anywhere in the 02:20:44

23 maternal blood? 02:20:46

24 MR. HOLMES: Objection. Vague. 02:20:49

25 THE WITNESS: We were unable to get fetal 02:20:50

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1 the foregoing is true and correct. Subscribed at
2 _____, California, this _____ day of
3 _____, 2012.

05:22:51

05:22:51

05:22:51

05:22:51

05:22:51

05:22:51

4
5
6 _____
7 MARK I. EVANS, M.D.

05:22:51

05:22:51

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2 **CERTIFICATE OF REPORTER**

3 I, **CATHERINE A. RYAN**, a Certified Shorthand
4 Reporter, hereby certify that the witness in the
5 foregoing deposition was by me first duly sworn to tell
6 the truth, the whole truth and nothing but the truth in
7 the within-entitled cause;

8 That said deposition was taken down in
9 shorthand by me, a disinterested person, at the time and
10 place therein stated, and that the testimony of the said
11 witness was thereafter reduced to typewriting, by
12 computer, under my direction and supervision;

13 That before completion of the deposition,
14 review of the transcript [☒] was [] was not requested.
15 If requested, any changes made by the deponent (and
16 provided to the reporter) during the period allowed are
17 appended hereto.

18 I further certify that I am not of counsel or
19 attorney for either or any of the parties to the said
20 deposition, nor in any way interested in the event of
21 this cause, and that I am not related to any of the
22 parties thereto.

23 DATED: April 30, 2012

24 Catherine A. Ryan
25 (CATHERINE A. RYAN, CSR NO. 8239)